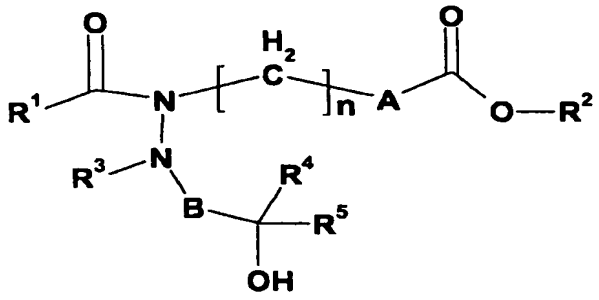
Claims

1. A hydrazide derivative of Formula (I):



(I)

as well as its geometrical isomers, its optically active forms as enantiomers, diastereomers and mixtures of these, as well as salts thereof, wherein:

A is selected from C_3-C_8 cycloalkyl, heterocycloalkyl, aryl and heteroaryl;

B is selected from C_1-C_6 alkylene, C_2-C_6 alkenylene, and C_2-C_6 alkynylene;

R^1 is selected from H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, heterocycloalkyl, aryl C_1-C_6 alkyl, heteroaryl C_1-C_6 alkyl, aryl and heteroaryl;

R^2 and R^3 are independently selected from H, C_1-C_6 alkyl, C_2-C_6 alkenyl and C_2-C_6 alkynyl.

R^4 is selected from hydrogen and C_1-C_6 alkyl;

R^5 is selected from hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 heteroalkyl, C_3-C_8 cycloalkyl, C_3-C_8 cycloalkyl C_1-C_6 alkyl, aryl C_1-C_6 alkyl, heteroaryl C_1-C_6 alkyl, aryl and heteroaryl;

n is an integer selected from 1, 2, 3, 4, 5 and 6.

2. A hydrazide derivative of claim 1 wherein A is selected from aryl and heteroaryl.

3. A hydrazide derivative according claims 1 or 2 wherein A is phenyl.

4. A hydrazide derivative according to any of the preceding claims wherein B is ethylene.

5. A hydrazide derivative according to any of the preceding claims wherein R^1 is C_1-C_6 alkyl.

6. A hydrazide derivative according to any of the preceding claims wherein R^2 is H.

7. A hydrazide derivative according to any of the preceding claims wherein R^3 is selected from H and methyl.

8. A hydrazide derivative according to any of the preceding claims wherein R^3 H.

9. A hydrazide derivative according to any of the preceding claims wherein R^4 is H.

10. A hydrazide according to any of the preceding claims wherein n is 2.

11. A hydrazide derivative according to any of the preceding claims wherein A is phenyl; B is ethylenyl; R^1 is C_1-C_6 alkyl; R^2 and R^4 are H; R^3 is selected from H and methyl; and n is 2.

12. A hydrazide derivative according to any of the preceding claims wherein R^5 is selected from H, C_1-C_6 alkyl and C_3-C_6 cycloalkyl

13. A hydrazide derivative according to any of the preceding claims wherein R^5 is aryl C_1-C_6 alkyl.

14. A hydrazide derivative according to any of the preceding claims wherein R^5 is heteroaryl C_1-C_6 alkyl.

15. A hydrazide derivative according to any of the preceding claims wherein R^5 is C_3-C_8 cycloalkyl.

16. A hydrazide derivative according to any of the preceding claims selected from the following group:

4-(2-{1-acetyl-2-[4-(3-chlorophenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
4-(2-{1-acetyl-2-[3-hydroxy-4-(3-iodophenyl)butyl] hydrazino}ethyl)benzoic acid;
4-(2-{1-acetyl-2-[4-(3-bromophenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
4-(2-{1-acetyl-2-[4-(1,1'-biphenyl-3-yl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
4-[2-(1-acetyl-2-{3-hydroxy-4-[3-(phenylethynyl)phenyl]butyl}hydrazino)ethyl] benzoic acid;
4-{2-[1-acetyl-2-(3-hydroxy-4-phenylbutyl)hydrazino]ethyl}benzoic acid;
4-(2-{1-acetyl-2-[4-(4-chlorophenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
4-(2-{1-acetyl-2-[4-(4-fluorophenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
4-(2-{1-acetyl-2-[4-(3-ethynylphenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
4-(2-{1-acetyl-2-[4-(3-fluorophenyl)-3-hydroxybutyl]hydrazino}ethyl)benzoic acid;
4-[2-(1-acetyl-2-{3-hydroxy-4-[4-(phenylethynyl)phenyl]butyl}hydrazino)ethyl] benzoic acid;
4-{2-[1-acetyl-2-(3-hydroxy-4-thien-2-ylbutyl)hydrazino]ethyl}benzoic acid;
4-[2-(1-acetyl-2-{4-[3-(cyclopropylethynyl)phenyl]-3-hydroxybutylhydrazino)ethyl] benzoic acid;
4-[2-(2-{3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl}-1-isobutyrylhydrazino)ethyl] benzoic acid;
4-[2-(2-{3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl}-1-propionylhydrazino)ethyl] benzoic acid;
4-[2-(1-acetyl-2-{3-hydroxy-4-[3-(trifluoromethyl)phenyl]butyl}hydrazino)ethyl] benzoic acid;
4-{2-[1-acetyl-2-(3-cyclohexyl-3-hydroxypropyl)hydrazino]ethyl}benzoic acid; or a pharmaceutically acceptable salt of any of said compounds.

17. A hydrazide derivative selected from the following group:
4-{2-[1-acetyl-2-(3-hydroxyoctyl)hydrazino]ethyl}benzoic acid;
4-{2-[1-acetyl-2-(3-hydroxyoctyl)-2-methylhydrazino]ethyl}benzoic acid;
4-{2-[1-acetyl-2-(3-hydroxybutyl)hydrazino]ethyl}benzoic acid;

or a pharmaceutically acceptable salt of any of said compounds.

18. A hydrazide derivative according to any of the preceding claims for use as a medicament.

19. A method for treating a disease or disorder associated with prostaglandins, comprising administering to a mammal suffering from or susceptible to such a disease or disorder an effective amount of a compound of any one of claims 1 through 17.

20. A method for treating a mammal is suffering from or susceptible to pre-term labor, dysmenorrhea, asthma, hypertension, undesired blood clotting, pre-elampsia, eclampsia, an eosinophil disorder, undesired bone loss, renal dysfunction, an immune deficiency disorder, dry eye, ichthyosis, elevated intra-ocular pressure, a gastric ulcer, fertility disorders, sexual dysfunction and inflammatory disorders comprising administering to the mammal an effective amount of a compound of any one of claims 1 through 17.

21. A method according to claims 19 or 20 wherein the mammal is suffering from or susceptible undesired muscle contraction.

22. A method according to claim 19 wherein the mammal is suffering from or susceptible to pre-term labor.

23. A method according to claims 19 or 20 wherein the mammal is suffering from or susceptible to a respiratory disease selected from asthma, chronic obstructive respiratory disease and emphysema.

24. A method of claims 19 or 20 wherein the mammal is suffering from or susceptible to hypertension.

25. A method of claims 19 or 20 wherein the mammal is suffering from or susceptible to bone loss.

26. A method of claims 19 or 20 wherein the mammal is suffering from or susceptible ovulatory disorders.

27. A method of claims 19 or 20 wherein the mammal is suffering from or susceptible erectile dysfunction.

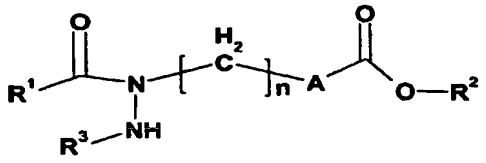
28. Use of a compound of any one of claims 1 through 17 for the preparation of a medicament to treat a disease or disorder associated with prostaglandin.

29. Use of a compound of any one of claims 1 through 17 for the preparation of a medicament to treat a disorder or a disease selected from preterm labor, dysmenorrhea, asthma, chronic obstructive respiratory disease, emphysema, hypertension, undesired blood clotting, preelampsia, eclampsia, an eosinophil disorder, undesired bone loss, renal dysfunction, an immune deficiency disorder, dry eye, ichthyosis, elevated intraocular pressure, gastric ulcers, fertility disorders, sexual dysfunction and inflammatory disorders.

30. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and one or more compounds of any one of claims 1 through 17.

31. A pharmaceutical composition of claim 30 wherein the compound is packaged together with instructions for use of the compound to treat a disorder or a disease selected from preterm labor, dysmenorrhea, asthma, hypertension, undesired blood clotting, a destructive bone disease or disorder, preeclampsia or eclampsia, an eosinophil disorder, renal dysfunction an immune deficiency disorder, dry eye, ichthyosis, elevated intraocular pressure and gastric ulcers.

32. A process for the preparation of a hydrazide derivative according to any of claims 1 to 17, comprising the step of a reductive amination of a hydrazide of Formula II with a compound of Formula III in presence of a reducing agent:



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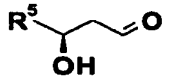
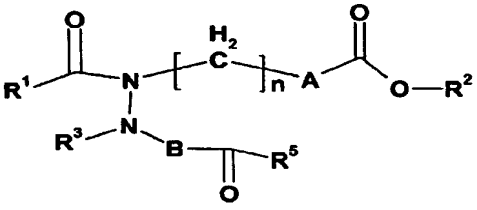


(III)

wherein A, R^1, R^2, R^3 and n are as defined above; R^5 is $-CH_2-R^6$ wherein R^6 is selected from C_1-C_5 alkyl, C_2-C_5 alkenyl, C_2-C_5 alkynyl, C_1-C_5 heteroalkyl, C_1-C_5 alkyl C_1-C_5 alkyl, aryl C_1-C_5 alkyl and heteroaryl C_1-C_5 alkyl.

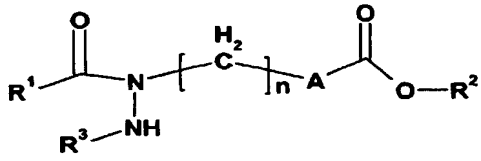
33. A process for the preparation of a hydrazide derivative according to any of claims 1 to 13, comprising the step of a reduction of a compound of Formula IV:



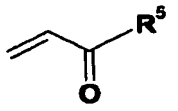
(IV)

wherein A, B, R^1, R^2, R^3, R^5 and n are as defined above.

34. A process of claim 29, further comprising the step of an addition of compound of Formula V to a compound of Formula II through a Michael addition:



(II)



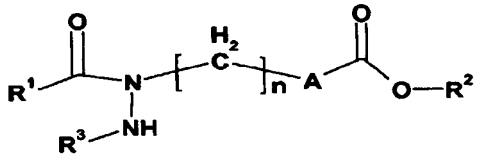
(V)

wherein A, B, R^1, R^2, R^3 and R^5 are as defined above; R^4 is H.

35. A process according to claims 32 to 34, further comprising the step of saponification of the resulting compound of Formula I wherein R^1 is not H into a compound of Formula I wherein R^2 is H.

36. A process according to claims 32 to 35 wherein A is phenyl.

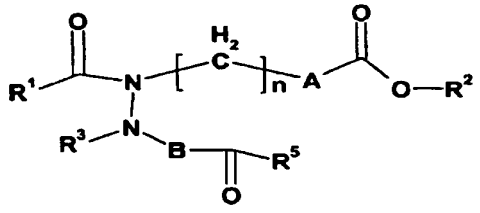
37. A compound of Formula II:



(II)

as well as its geometrical isomers, its optically active forms as enantiomers, diastereomers and mixtures of these, as well as salts thereof, wherein A, R^1, R^2, R^3 and n are as defined above.

38. A compound of Formula IV:



(IV)

as well as its geometrical isomers, its optically active forms as enantiomers, diastereomers and mixtures of these, as well as salts thereof, wherein A, R^1, R^2, R^3, R^5 and n are as defined above.